Testosterone Replacement Therapy in Hypogonadal Men at High Risk for Prostate Cancer: Results of 1 Year of Treatment in Men With Prostatic Intraepithelial Neoplasia

Rhoden EL, Morgentaler A.

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The practice of Rhoden and Morgentaler is to perform prostate needle biopsy in all patients who are prescribed androgen replacement therapy, thus providing a unique opportunity to identify patients who have abnormal prostate histology and follow them during replacement therapy. In this report, the investigators compare the results of serum prostate-specific antigen (PSA) evaluation and rectal examination at baseline and 1 year after initiation of androgen replacement among patients with (n = 20) and without (n = 50) PIN.

The authors noted no significant differences between the 2 groups in regard to mean baseline PSA or serum testosterone levels. For purposes of this study, a serum total testosterone level of less than 300 ng/dL was considered to be subnormal. During the course of therapy, patients who were noted to have a rise in PSA of greater than 1.0 ng/dL or who manifested an alteration in rectal examination results underwent repeat prostate needle biopsy. Using these parameters, 4 men in the group without PIN underwent biopsy (all of which were negative). Two patients in the group with PIN qualified for biopsy based on increasing PSA level; one of these men refused the procedure. An additional patient in the PIN group was noted to have an abnormal rectal examination result and was found to have prostate cancer on biopsy.

PIN does not appear to be a contraindication for the use of androgen replacement therapy among hypogonadal men.

It was also noted that the increase in serum PSA level at 1 year versus baseline was not significantly different between patients without PIN and those with PIN (0.25 ng/dL and 0.35 ng/dL, respectively). Although the authors acknowledge that this study includes a relatively small cohort of patients and is limited by the duration of follow-up, they conclude that PIN does not appear to be a contraindication for the use of androgen replacement therapy among hypogonadal men.

Certainly, additional investigation is needed to more fully assess whether androgen replacement therapy poses increased risk as it pertains to prostate malignancy. Because this study examines a population at high risk for prostate cancer, its results are of particular interest. These data are one more piece of the clinical puzzle of androgen replacement therapy in the aging man. ■

Incontinence

Estrogen for Overactive Bladder and Patient Perception of Incontinence

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A Double-Blind Placebo-Controlled Trial on the Effects of 25 mg Estradiol Implants on the Urge Syndrome in Postmenopausal Women

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Over the past 12 months, estrogen has been battered in the medical and public press because of the controversy that an increased risk of cancer may outweigh any beneficial clinical effect. Nevertheless, estrogen remains a commonly prescribed therapy for both stress and urge incontinence. Is the use of estrogen in this setting justified?

The aim of this prospective, double-blind, randomized, placebo-controlled trial was to determine the effect of systemic estrogen on the "urge syndrome" in postmenopausal women. The study was conducted in the urogynecology unit at King's College Hospital in London, UK.

Forty postmenopausal women with the urge syndrome were randomly allocated to receive a 25-mg 17ß-estradiol implant or a placebo implant. Serum estradiol levels and endometrial thickness were measured before and after treatment at 1, 3, and 6 months. Outcome measures included videocystourethrography, frequency volume chart, visual analogue score of symptoms, and the King's Health Care

Quality of Life Questionnaire.

Subjectively, both groups experienced a significant improvement in urgency, and the estradiol group experienced a significant improvement in urge incontinence; however, there were no significant differences between the groups. Objectively, no significant differences were demonstrated between the groups. Nine women in the estradiol group experienced vaginal bleeding, of whom 5 required a hysterectomy during or after the study.

Despite the use of numerous outcome measures, the 25-mg estradiol implant did not produce a greater improvement in urgency symptoms compared with placebo. In addition, the estradiol implant was associated with a high complication rate. These results make it is difficult justify the use of estrogen for overactive bladder symptoms. Although estrogen may play a role in reducing the discomfort and irritation associated with atrophic vaginal tissue, it appears to have no use in the treatment of bladder urgency symptoms.

Relationship Between Patient Report and Physician Assessment of Urinary Incontinence Severity

Melville JL, Miller EA, Fialkow MF, et al.

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How severe is your patient's incontinence? Does a patient know when her urinary incontinence is severe versus mild? The purpose of this study was to determine the relationship between patient report and physician assessment of urinary incontinence severity. A total of 153 women with urinary incontinence completed a detailed health questionnaire that included a medical comorbidity scale, the 12-item short-form health survey (SF-12), the incontinence quality of life instrument, the Primary Care Evaluation of Mental Disorders (PRIME-MD) Patient Health Questionnaire, and a patient incontinence severity assessment. The study was carried out at the University of Washington's Department of Obstetrics and Gynecology in Seattle.

The patient incontinence severity assessment is a single question that asks the patient to rate the severity of her incontinence symptoms on a 5-point Likert scale (range, 1 [mild] to 5 [severe]). In addition, the physicians assigned each patient a physician incontinence severity assessment score, which rates the severity of the patient's incontinence on a 5-point Likert scale (range, 1 [mild] to 5 [severe]).

The study found a high correlation between patient report and physician assessment of urinary incontinence severity. Both patient report (patient incontinence severity assessment) and physician assessment (physician incontinence severity assessment) correlated well with a validated severity index. The agreement between patient and physician ratings was highest for mild incontinence but decreased as incontinence severity progressed.

Most urologists would likely agree with the conclusions of this study. When symptoms are mild to moderate, the patient history is clear and empiric treatment is often successful. When leakage is severe, it becomes difficult to differentiate between urge and stress incontinence. We have all heard statements such as "I don't know when I leak" or "I leak all of the time." These situations are frustrating for both patients and doctors. Careful patient assessment, including urodynamic evaluation, is most helpful in these instances. ■

Prostate Cancer

Vitamin D for the Management of Prostate Cancer

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Although vitamin D can be obtained from many natural dietary sources, such as fish liver oil, eggs, and dairy products, for the majority of men, this dietary source fails to meet the daily required levels.[1,2] Instead, their major source of vitamin D is derived from synthesis in the skin through conversion of a precursor (7-dehydrocholesterol) into vitamin D_3, a reaction catalyzed by ultraviolet light present in sunlight.[2] Vitamin D_3 subsequently undergoes hydroxylation in the liver followed by the kidney, resulting in the synthesis of 1,25-dihydroxyvitamin D_3, or calcitriol, which is the principal active hormonal form of vitamin D.[2]

In addition to its well-known role in regulating calcium homeostasis in the body via its actions in the kidney, bone, intestine, and parathyroid glands,[2] vitamin D also exhibits antitumorigenic properties, as demonstrated in in-vivo studies.[3] This knowledge has led to epidemiologic studies investigating the association between vitamin D deficiency and prostate cancer. Accordingly, Schwartz and Hulka[4] were the first to propose that low levels of vitamin D increase the risk of prostate cancer. These observations were based on